Derivatives of Piperazine. XV.
The Kindler Modification of the Willgerodt Reaction Using Phenylpiperazines

By

JOHN CHARLES BRAUN

A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA
August, 1955

25

CONTENTS

Page

LIST OF TABLES iv

Chapter

I. REVIEW OF THE LITERATURE 1

Introduction 1
Mechanism 3

II. EXPERIMENTAL WORK 7

Reactants and Reaction Solvents 7
Preparation of 1-Aryl-4-thioalkanoylpiperazines and 1-Aryl-4-thioaroylpiperazines 7
Purification of Products 9
Thioaroyl Derivatives 9
Thioalkyl Derivatives 11
Description of Compounds 12
1-Phenyl-4-(thiobutanoyl)piperazine 13
1-Phenyl-4-(thioisobutanoyl)piperazine 14
1-Phenyl-4-(thiopentanoyl)piperazine 15
1-Phenyl-4-(thiohexanoyl)piperazine 16
1-Phenyl-4-(2-ethylthiobutanoyl)piperazine 17
1-Phenyl-4-(4-methylthiopentanoyl)piperazine 18
1-Phenyl-4-(thioheptanoyl)piperazine 19
1-Phenyl-4-(thioöctanoyl)piperazine 20
1-Phenyl-4-(thiononanoyl)piperazine 21
1-Phenyl-4-(thiodecanoyl)piperazine 22
1-Phenyl-4-(thiobenzoyl)piperazine 23
1-Phenyl-4-(thio-2-thenoyl)piperazine 24
1-Phenyl-4-(phenylthioacetyl)piperazine 25
1-Phenyl-4-(thio-*p*-anisoyl)piperazine 26
1-Phenyl-4-(thiopiperonyloyl)piperazine 27
1-Phenyl-4-(thioveratroyl)piperazine 28
1-Phenyl-4-(1-naphthylthioacetyl)piperazine 29
1-(*o*-Tolyl)-4-(thiobutanoyl)piperazine 30
1-(*o*-Tolyl)-4-(thiobenzoyl)piperazine 31
1-(*o*-Tolyl)-4-(thio-2-thenoyl)piperazine 32
1-(*o*-Tolyl)-4-(phenylthioacetyl)piperazine 33

CONTENTS (Continued)

Chapter Page

1-(*o*-Tolyl)-4-(thio-*p*-anisoyl)piperazine 34
1-(*o*-Tolyl)-4-(thiopiperonyloyl)piperazine 35
1-(*o*-Tolyl)-4-(2-naphthylthioacetyl)piperazine . . . 36
1-(*m*-Tolyl)-4-(thiobenzoyl)piperazine 37
1-(*m*-Tolyl)-4-(phenylthioacetyl)piperazine 38
1-(*m*-Tolyl)-4-(thioveratroyl)piperazine 39
1-(*m*-Tolyl)-4-(1-naphthylthioacetyl)piperazine . . . 40
1-(*p*-Tolyl)-4-(thiobenzoyl)piperazine 41
1-(*p*-Tolyl)-4-(thio-2-thenoyl)piperazine 42
1-(*p*-Tolyl)-4-(phenylthioacetyl)piperazine 43
1-(*p*-Tolyl)-4-(thiopiperonyloyl)piperazine 44
1-(*p*-Tolyl)-4-(thioveratroyl)piperazine 45
1-(*o*-Chlorophenyl)-4-(thiobenzoyl)piperazine 46
1-(*o*-Chlorophenyl)-4-(thio-2-thenoyl)piperazine. . . . 47
1-(*o*-Chlorophenyl)-4-(phenylthioacetyl)piperazine. . 48
1-(*o*-Chlorophenyl)-4-(thiopiperonyloyl)piperazine. . 49
1-(*o*-Chlorophenyl)-4-(1-naphthylthioacetyl)-piperazine 50
1-(*m*-Chlorophenyl)-4-(thiobenzoyl)piperazine 51
1-(*m*-Chlorophenyl)-4-(thio-2-thenoyl)piperazine . . 52
1-(*m*-Chlorophenyl)-4-(thiopiperonyloyl)piperazine. . . 53
1-(*m*-Chlorophenyl)-4-(thioveratroyl)piperazine . . . 54
1-(*m*-Chlorophenyl)-4-(1-naphthylthioacetyl-piperazine 55
1-(*p*-Chlorophenyl)-4-(thiobenzoyl)piperazine 56
1-(*p*-Chlorophenyl)-4-(thio-2-thenoyl)piperazine . . 57
1-(*p*-Chlorophenyl)-4-(thiopiperonyloyl)piperazine. . 58
1-(*p*-Chlorophenyl)-4-(1-naphthylthioacetyl-piperazine 59

III. SUMMARY 60

BIBLIOGRAPHY 65

BIOGRAPHICAL ITEMS 68

ACKNOWLEDGEMENTS 69

LIST OF TABLES

Table | Page
I. Physical and Analytical Data of Thioamides from Piperazines 61

CHAPTER I

REVIEW OF THE LITERATURE

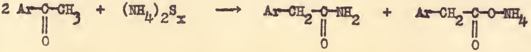
Introduction

The first thioamide, thiobenzamide, was prepared in 1848 by Cahours by bubbling hydrogen sulfide through an ammoniacal ethanol solution of benzonitrile.[6] He named it "benzamide sulfuré" because of its analog in the amide series discovered several years previously by Dumas.[15]

The Willgerodt reaction receives its name from Conrad Willgerodt, who first used it in 1887 in the preparation of 1-naphthylacetamide.[42] The reaction consists of heating an arylmethyl ketone in a saturated aqueous solution of ammonium polysulfide inside a sealed tube for periods ranging from a few hours to two or three days.

After the reaction mixture has cooled the solid portion is subjected to fractional recrystallizations. Besides a quantity of tarry residue, there is found an amide of an acid having the same carbon skeleton as the ketone used. It is accompanied by varying amounts of the ammonium salt of the acid.

The reaction may be represented by the equation:



$$2\ Ar-\underset{\underset{O}{\|}}{C}-CH_3 + (NH_4)_2S_x \longrightarrow Ar-CH_2-\underset{\underset{O}{\|}}{C}-NH_2 + Ar-CH_2-\underset{\underset{O}{\|}}{C}-O-NH_4$$

It was discovered later by Kindler that a thioamide resulted when the aqueous ammonium sulfide solution was replaced by sulfur and an anhydrous amine or ammonia.[23] As in the Willgerodt reaction, the carbonyl group was reduced, and the functional group is on the terminal carbon atom.

The two reactions have proven to be quite versatile. It has been found that aldehydes,[14, 23, 42] unsaturated hydrocarbons,[7,8] ketones,[21] mercaptans,[31,32] ketoacid esters,[20] disulfides,[31] secondary alcohols,[32] amines,[4,19,23,41] and even some aralkyl hydrocarbons[33] and picolines,[38] react. Although it was thought for a long time that the reactions were confined to the aromatic series, it has been found that, except for saturated hydrocarbons, the same types of compounds in the aliphatic series also react, but generally with lower yields.[10,11] Aromatic ketones with longer alkyl chains react, but yields become progressively less as the chain length increases.[42-45] When the alkyl chain is branched, yields are also decreased.[42-45] A quaternary carbon atom in the chain has been found to prevent the reaction.[27] Attempts to react arylalkyl ketones having more than five carbon atoms in the chain and some attempts with branched-chain ketones have resulted either in cleavage of the chain or in reduction to the parent hydrocarbon.[1,27,45]

Products of this reaction have been reported as having the following substitutents on the aromatic ring: hydroxy, nitro, amino, acylamino, methoxy, alkyl, and halogens.[2,12,25,29] Yields of para-substituted products have been reported to decrease in the order:

hydrogen, hydroxy, iodo, methoxy, chloro, methyl.[2] The presence of these substituents apparently favors the formation of substituted thiophenes. These were found in increasing quantities as yields of the desired products decreased.[2]

Kindler found that N-benzyl-arylmethenimines are converted to thioamides when heated with sulfur.[23]

It was found by Baumann and Fromm that many of the compounds which undergo these reactions will also react with sulfur to form substituted thiophenes. These and the unreacted sulfur, from which it is almost impossible to separate them, constitute the bulk of the tarry material always found.[3]

Purified propanol-2, dioxane, or pyridine has been used as a solvent to increase the mutual solubility of the reactants and to decrease reaction temperatures. Yields are increased because less of the tarry by-products is formed at the lower temperature.[14,17,34] Pyridine containing picolines, however, results in even more impurities. As has been mentioned, some of the picolines undergo the reaction. A polymerization reaction has also been found to occur between sulfur and α-picoline.[16]

High-boiling amines, such as morpholine and piperazine, have been used for the Kindler reaction at atmospheric pressure.[12,39]

Mechanism

Willgerodt proposed that the oxygen atom wandered to the chain end, where it exchanged places with two hydrogen atoms, and that the aldehyde then reacted with the sulfur and ammonia to form the amide and hydrogen sulfide.[42]

Kindler suggested a mechanism involving a shift of the aryl group to the terminal carbon.[23,25] Recent experiments with acetophenones labeled with radioactive carbon atoms, as well as experiments by Willgerodt and later workers with branched-chain aryl ketones, prove that there is no change in the carbon skeleton of the reacting compounds except for chain rupture in the case of very long or of some branched chains.[1,8,11,13,43,45]

Carmack and DeTar proposed a mechanism including a phenylacetylene as an intermediate.[9,14] Their own work, however, resulted in lower yields from phenylacetylene than from acetophenone.[7] The fact that branched-chain compounds give the expected products also argues against this mechanism, since an acetylenic structure could not proceed past a tertiary carbon atom. Different mechanisms are needed, therefore, for straight and branched-chain structures.

King and McMillan propose a mechanism with phenyl olefins as intermediate products.[27,28] Their own work, resulting in approximately the same yields from styrene and from acetophenone, supports this mechanism.[26] Other investigators, however, have obtained greater yields from acetophenone than from styrene.[7,46]

Yukawa and Kishi, as well as Yukawa, Tokuda, and Amano, have proposed mechanisms in which a polysulfide ring connects the terminal and carbonyl carbon atoms.[46,47] This is supported by the work of Carmack and DeTar in which best yields were obtained by a ten-fold excess of sulfur.[14]

The mechanism of McMillan and King assumes an initial addition of hydrogen sulfide to the olefin produced by dehydration and reduction of the ketone.[27,28]

The mechanisms of Carmack and DeTar[9,14] and of Yukawa and his co-workers[46,47] begin with the addition of ammonia or amine to the carbonyl group.

That either sulfur or ammonia could initiate the reaction is supported by the work of Baumann and Fromm, who found that sulfur reacts with acetophenone even at room temperature,[3] and of Thomae, who reacted ammonia with acetophenone at room temperature.[40]

An amine could not react as far with acetophenone as does ammonia [to form the compound $(C_6H_5O{-}CH_3)_3N_2$] but could react with one molecule of the ketone to form the 1-phenyl-1-aminoethanol proposed as the first intermediate compound.

The mechanism of Yukawa and Kishi[46] proposes a direct conversion of a disulfide to a thioamide, while that of Yukawa, Tokuda, and Amano[47] suggests the addition of the amine to the thioaldehyde and then rearrangement to form the thioamide.

King and McMillan proposed the sequence of mercaptan to thioaldehyde to dithio acid,[27] but in a later paper they suggested that the mercaptan is first converted to the disulfide and then to a series of five intermediate compounds between the disulfide and the thioamide.[31] A thiohydroxylamine, which might result from the reaction of sulfur with the amine present in the reaction mixture, would react with the disulfide. This reaction would produce two molecules of the same type of compound as would be formed by the condensation of two molecules of the secondary amine with the aldehyde having the same carbon skeleton as the mercaptan, $ArCH_2CH(NR_2)_2$.[18] This compound, by means of another rather complicated mechanism, adds a sulfur atom and loses an amine molecule (as separate ions) to form the thioamide.

None of these mechanisms can be discarded because of its simplicity or its complexity or because some compound which has been proposed as an intermediate has failed to produce as much yield as the ketone in question did. Further studies of the reaction from the kinetic viewpoint are needed before the details of the mechanism can be established.

It has been established that yields are decreased by increasing the concentration of hydrogen sulfide[14] and increased by increasing the concentrations of either sulfur or amine.[14,24,28,39] The addition of sodium or ammonium thiosulfate has also been found to increase yields.[35] This indicates that ammonium thiosulfate or an amine thiosulfate may be formed in the reaction mixture and that it acts as a catalyst at some stage of the reaction.

CHAPTER II

EXPERIMENTAL WORK

Reactants and Reaction Solvents

1-Phenylpiperazine was prepared by the method of Pollard and MacDowell.[36]

1-(Chlorophenyl)piperazines and 1-(tolyl)piperazines were prepared by the method of Pollard and Wicker.[37]

Aldehydes and ketones were purchased from various chemical supply firms; C. P. grades were purchased when available, and no attempt was made at purification of even the technical grades.

Karl Fischer reagent grade pyridine was used as solvent for the reaction. [Technical grade pyridine used at first gave excessive amounts of tarry by-products, as did dioxane.]

U.S.P. Flowers of sulfur was used. [The technical grade sulfur used in preliminary experiments left a residue when burned and was suspected of contributing to the tarry impurities contaminating the products.]

Preparation of 1-Aryl-4-thioalkanoylpiperazines and 1-Aryl-4-thioaroylpiperazines

The compounds described in this dissertation were all prepared in exactly the same way. In every case equimolar quantities of all reactants were used (0.1 mole). Preliminary tests in the preparation of the same compound resulted in negligible differences in yields between reactions terminated after two to three hours and those allowed to proceed for an entire day. No effort was made, therefore, to place any definite limit on reaction time or to make any note of the times, other than to make certain that each was at least two hours.

Since the descriptions of the preparations are all identical, except for the weights or volumes of the aldehyde or ketone and of the phenylpiperazine used, a single complete description will be given. The weights and volumes of reactants are listed for each preparation on the page describing that compound.

The reactions were carried out in 200-ml., round-bottomed flasks attached by standard tapers to reflux condensers.

One-tenth of a mole (3.2 g.) of sulfur and a carborundum boiling chip were placed in the flask. This was followed by part of the pyridine and the calculated quantities of the phenylpiperazines and the aldehyde or ketone. The flask was swirled gently during the addition of the liquid reagents, after which sufficient pyridine was added to fill the flask about three-fourths full. Any sulfur or other reactant was rinsed out of the neck of the flask as the pyridine was added. The flask, which became hot quite rapidly when an aldehyde was one of the reactants, was immediately connected to the condenser without grease on the joint. Heat was applied, either by a heating mantle or by an especially built heater, and the liquid was refluxed slowly for at least two hours.

In reactions with aldehydes the solutions turned dark brown immediately, while those with ketones did so only after they had been heated for some time. As the reaction progressed, all the sulfur disappeared and some hydrogen sulfide was evolved. For this reason, a hood or adequate ventilation is necessary. Small quantities of sublimed solid were usually found in the condensers. No attempt has been made to determine whether this solid was sulfur or a reaction product, since the desired products showed little volatility even at pressures as low as 2 mm. Hg.

Purification of Products

The purification of substituted thioamides is quite involved. The procecures required for derivatives of aromatic thioacids are entirely different from those required for derivatives of aliphatic thioacids. A complete description will be given only for the method found most suitable for each type, rather than separate descriptions of all the methods tried, since many trials proved to be wasteful of both time and product.

Thioaroyl Derivatives

These products are generally of very limited solubilities and were obtained in fairly pure condition by pouring the contents of the reaction flask into a beaker containing 400-500 ml. of 95 per cent ethanol and allowing the beaker to cool slowly. Some compounds did not crystallize for several hours.

When crystals had formed they were removed by suction-filtration, returned to the beaker, rinsed thoroughly with ethanol, and collected again. Repeated recrystallizations from ethanol, with decolorizing charcoal used when necessary, generally resulted in analytically pure samples.

Those compounds having very limited solubilities in ethanol were dissolved in an acetone-ethanol mixture. This had the disadvantages of dissolving unreacted sulfur and other impurities to a greater extent than did ethanol and of preventing much decolorization by the charcoal.

The rinsings and mother liquors were added to the dark-colored liquid containing the remaining part of the reaction mixture, heated with charcoal (and with fuller's earth if it obviously had an abnormally large quantity of dark impurities), and filtered while hot — first through a very coarse paper to permit fast filtration and remove the bulk of the charcoal and then through fine paper to remove the small amount of charcoal remaining. If the solution was still very dark, it proved best to add water until the solution became faintly turbid and then allow it to cool. When this solution was cooled in an ice bath the crystals were smaller and often were accompanied by sufficient impurities to produce a thick, gummy mass. However, most of the dark-colored impurities remained in the solution. When the solid was dissolved in alcohol most of the unreacted sulfur remained undissolved except in the cases of extremely insoluble products which required prolonged refluxing with ethanol or the addition of acetone.

The ethanol solution was decolorized much more readily by charcoal than was the solution which contained pyridine. It was found that charcoal decolorized products of this type best in heptane or hexane solutions. Decolorization decreased progressively with ethanol, propanol-2, aromatic hydrocarbons, acetone, and pyridine. If very much of either of the last three liquids was used in a solution, effective decolorization was prevented.

Other impurities which contaminated the aromatic type products were the sulfide salts of the unreacted phenylpiperazines. The compounds were soluble, or moderately soluble, in acetone, while the salts were only very slightly soluble. Therefore, these impurities were generally removed by one recrystallization from an acetone-water solution. The product was dissolved in acetone, and water was then added to the hot solution to the point of slight turbidity. As the solution cooled the thioamide crystallized, while the sulfide salts, most of which were very soluble in water, remained in solution. However, p-chlorophenylpiperazine sulfide, which is quite insoluble in either water or ethanol, could be removed only by repeated recrystallizations.

The thioamides of this type, which are all some shade of yellow or orange, were generally slightly lighter colored, smaller crystals when they were crystallized from acetone-water than when recrystallized from ethanol.

Thioalkyl Derivatives

These are usually low-melting, very soluble compounds which must, therefore, be purified by an entirely different procedure. Pyridine dissolved them so readily that its removal by steam distillation proved advisable. The non-aqueous layer was then extracted several times with boiling hexane. The products were readily dissolved, but very little of the dark impurities and almost no sulfur was extracted. A small amount of charcoal readily removed the impurities that did dissolve. Concentration of the solution, followed by chilling in an ice bath, usually caused the product to crystallize. Occasionally, however, a dry ice-propanol-2 bath was necessary. The compound was then recrystallized several times from ethanol-water or ethanol solutions. The dry ice bath was nearly always needed for these recrystallizations. Some of the compounds retained enough adsorbed liquid to dissolve them completely, even below room temperature, and were put in a vacuum desiccator while still cold. The desiccator was evacuated first by a water aspirator, then by vacuum pump, and a cold trap was used to collect the solvent.

Description of the Compounds

Data on the compounds prepared during this research are tabulated on the pages which follow.

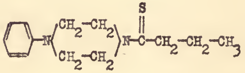
Melting points are given in degrees Centigrade, corrected; the abbreviation "°C." is omitted.

Since equimolar quantities were used, yield calculations may be based upon either reactant. The yield figures actually reflect difficulty of purification more than success of the reaction.

All analyses were done by Geller Microanalytical Laboratories, Hackensack, N. J.

1-Phenyl-4-(thiobutanoyl)piperazine

Graphic Formula:



Reactants:		
	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Butanal	8.7 ml., 7.2 g.
	Sulfur	3.2 g.

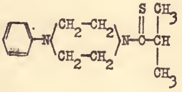
Reaction Solvent	Pyridine
Yield, %	29
Molecular Formula	$C_{14}H_{20}N_2S$
Molecular Weight	248.38
Melting Point	66.8-67.8
Analysis: Nitrogen, %	Calcd., 11.28; Found, 11.35
Crystals (pale yellow plates)	from Ethanol-Water

Solubilities:

Very soluble in	Acetone
Very soluble in	Ethanol
Soluble in	Hexane
Insoluble in	Water

1-Phenyl-4-(thioisobutanoyl)piperazine

Graphic Formula:



Reactants:

1-Phenylpiperazine	16.0 ml., 16.2 g.
Isobutanal	9.1 ml., 7.2 g.
Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 50

Molecular Formula . . . . $C_{14}H_{20}N_2S$

Molecular Weight 248.38

Melting Point 62.7-63.7

Analysis: Nitrogen, % . . . . . Calcd., 11.28; Found, 11.12

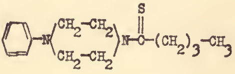
Crystals (pale yellow flakes) . . . . from Ethanol

Solubilities:

Very soluble in	Acetone
Very soluble in	Ethanol
Soluble in	Hexane
Insoluble in	Water

1-Phenyl-4-(thiopentanoyl)piperazine

Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Pentanal	10.4 ml., 8.6 g.
	Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 13

Molecular Formula . . . . $C_{15}H_{22}N_2S$

Molecular Weight 262.41

Melting Point 47.5-48.5

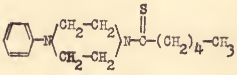
Analyses:	Carbon, %	Calcd., 68.65; Found, 68.82
	Hydrogen, %	Calcd., 8.45; Found, 8.52

Crystals (ivory flakes) . . . . from Ethanol-Water

Solubilities:	Very soluble in	Acetone
	Soluble in	Ethanol
	Moderately soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(thiohexanoyl)piperazine

Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Hexanal	12.0 ml., 10.0 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	14
Molecular Formula	$C_{16}H_{24}N_2S$
Molecular Weight	276.43
Melting Point	62.7-63.7

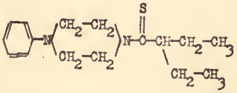
Analyses:	Carbon, %	Calcd., 69.51	Found, 69.75
	Hydrogen, %	Calcd., 8.75	Found, 8.77

Crystals (ivory flakes)	from Ethanol

Solubilities:	Very soluble in	Acetone
	Very soluble in	Ethanol
	Very soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(2-ethylthiobutanoyl)piperazine

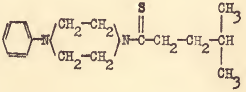
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	2-Ethylbutanal	13.0 ml., 10.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		30
Molecular Formula		$C_{16}H_{24}N_2S$
Molecular Weight		276.43
Melting Point		94-95
Analyses:	Carbon, %	Calcd., 69.51; Found, 69.70
	Hydrogen, %	Calcd., 8.75; Found, 8.70
Crystals (long yellow needles)		from Heptane
Solubilities:	Very soluble in	Acetone
	Soluble in	Ethanol
	Moderately soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(4-methylthiopentanoyl)piperazine

Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Methylisobutyl ketone	12.5 ml., 10.1 g.
	Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 5

Molecular Formula . . . . $C_{16}H_{24}N_2S$

Molecular Weight 276.43

Melting Point 77.8-78.8

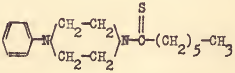
Analyses:	Carbon, %	Calcd., 69.51; Found, 68.84
	Hydrogen, %	Calcd., 8.75; Found, 8.65

Crystals (pale yellow flakes) . . . . from Ethanol

Solubilities:	Very soluble in	Acetone
	Very soluble in	Ethanol
	Soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(thioheptanoyl)piperazine

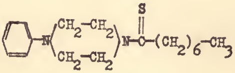
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Heptanal	13.4 ml., 11.4 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		14
Molecular Formula		$C_{17}H_{26}N_2S$
Molecular Weight		290.46
Melting Point		62.7-63.7
Analyses:	Carbon, %	Calcd., 70.29; Found, 70.57
	Hydrogen, %	Calcd., 9.02; Found, 8.82
Crystals (ivory flakes)		from Ethanol
Solubilities:	Very soluble in	Acetone
	Soluble in	Ethanol
	Moderately soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(thioöctanoyl)piperazine

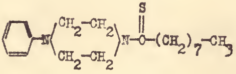
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Octanal	17.4 ml., 12.8 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		25
Molecular Formula		$C_{18}H_{28}N_2S$
Molecular Weight		304.48
Melting Point		48.5-49.5
Analyses:	Carbon, %	Calcd., 71.00; Found, 70.98
	Hydrogen, %	Calcd., 9.27; Found, 9.30
Crystals (very pale yellow powder)		from Ethanol
Solubilities:	Very soluble in	Acetone
	Very soluble in	Ethanol
	Very soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(thiononanoyl)piperazine

Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	n-Nonanal	17.2 ml., 14.2 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	28
Molecular Formula	$C_{19}H_{30}N_2S$
Molecular Weight	318.51
Melting point	52.6-53.6

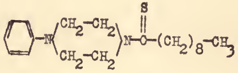
Analyses:	Carbon, %	Calcd., 71.64;	Found, 71.41
	Hydrogen, %	Calcd., 9.49;	Found, 9.21

Crystals (pale yellow flakes)	from Ethanol

Solubilities:	Very soluble in	Acetone
	Soluble in	Ethanol
	Moderately soluble in	Hexane
	Insoluble in	Water

1-Phenyl-4-(thiodecanoyl)piperazine

Graphic Formula:



Reactants: 1-Phenylpiperazine . . . . 16.0 ml., 16.2 g.

n-Decanal . . . . 18.8 ml., 15.6 g.

Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 36

Molecular Formula . . . . $C_{20}H_{32}N_2S$

Molecular Weight 332.54

Melting Point 51.6-52.6

Analyses: Carbon, % . . . . . . Calcd., 72.23; Found, 71.90

Hydrogen, % . . . . . Calcd., 9.70; Found, 9.85

Crystals (fluffy, very small cream flakes) . . . . from Ethanol

Solubilities: Very soluble in . . . . Acetone

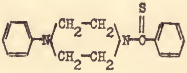
Very soluble in . . . . Ethanol

Very soluble in . . . . Hexane

Insoluble in . . . . Water

1-Phenyl-4-(thiobenzoyl)piperazine

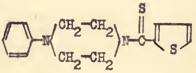
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		83
Molecular Formula		$C_{17}H_{18}N_2S$
Molecular Weight		282.39
Melting Point		93.5-94.5
Analyses:	Nitrogen, %	Calcd., 9.92; Found, 9.73
	Sulfur, %	Calcd., 11.35; Found, 11.75
Crystals (yellow needles)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(thio-2-thenoyl)piperazine

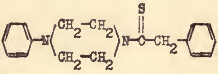
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Thiophene aldehyde	9.2 ml., 11.2 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		35
Molecular Formula		$C_{15}H_{16}N_2S_2$
Molecular Weight		288.42
Melting Point		106.1-107.1
Analyses:	Carbon, %	Calcd., 62.46; Found, 62.75
	Hydrogen, %	Calcd., 5.59; Found, 5.71
	Nitrogen, %	Calcd., 9.71; Found, 9.45
Crystals (shiny, deep orange plates)		from Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(phenylthioacetyl)piperazine

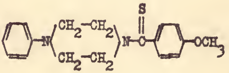
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Acetophenone	11.6 ml., 12.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		62
Molecular Formula		$C_{18}H_{20}N_2S$
Molecular Weight		296.42
Melting Point		125.2-126.2
Analysis:	Nitrogen, %	Calcd., 9.45; Found, 9.42
Crystals (beige needles)		from Ethanol
Solubilities:		
	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(thio-p-anisoyl)piperazine

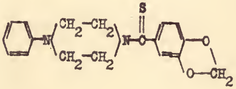
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	p-Anisaldehyde	12.1 ml., 13.6 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		61
Molecular Formula		$C_{18}H_{20}ON_2S$
Molecular Weight		312.42
Melting Point		160.2-161.7
Analyses:	Carbon, %	Calcd., 69.19; Found, 69.75
	Hydrogen, %	Calcd., 6.45; Found, 6.64
Crystals (lustrous yellow plates)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(thiopiperonyloyl)piperazine

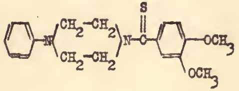
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		65
Molecular Formula		$C_{18}H_{18}O_2N_2S$
Molecular Weight		326.40
Melting Point		130.3-131.3
Analysis:	Nitrogen, %	Calcd., 8.58; Found, 8.76
Crystals (bright yellow powder)		from Acetone-Water
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(thioveratroyl)piperazine

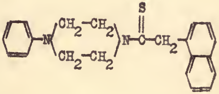
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	Veratraldehyde	16.7 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		70
Molecular Formula		$C_{19}H_{22}O_2N_2S$
Molecular Weight		342.45
Melting Point		160.7-162.7
Analyses:	Carbon, %	Calcd., 66.63; Found, 67.01
	Hydrogen, %	Calcd., 6.48; Found, 6.66
Crystals (shiny yellow plates)		from Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-Phenyl-4-(1-naphthylthioacetyl)piperazine

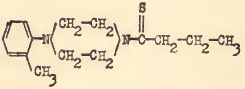
Graphic Formula:



Reactants:	1-Phenylpiperazine	16.0 ml., 16.2 g.
	1-Acetonaphthone	16.0 ml., 17.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		14
Molecular Formula		$C_{22}H_{22}N_2S$
Molecular Weight		346.48
Melting Point		134.7-136.2
Analysis:		
	Nitrogen, %	Calcd., 8.09; Found, 8.29
Crystals (pale yellow powder)		from Acetone-Ethanol
Solubilities:		
	Slightly soluble in	Acetone
	Very slightly soluble in	Ethanol
	Insoluble in	Water

1-(o-Tolyl)-4-(thiobutanoyl)piperazine

Graphic Formula:



Reactants: 1-(o-Tolyl)piperazine . . . . . 17.0 ml., 17.6 g.

n-Butanal . . . . 8.7 ml., 7.2 g.

Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 38

Molecular Formula . . . . $C_{15}H_{22}N_2S$

Molecular Weight 262.41

Melting Point 71.8– 72.8

Analyses: Carbon, % . . . . . . Calcd., 68.65; Found, 67.84

Hydrogen, % . . . . . Calcd., 8.45; Found, 8.35

Crystals (pale yellow flakes) . . . . from Ethanol

Solubilities: Very soluble in . . . . Acetone

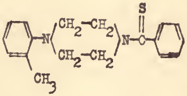
Soluble in . . . . Ethanol

Soluble in . . . . Hexane

Insoluble in . . . . Water

1-(*o*-Tolyl)-4-(thiobenzoyl)piperazine

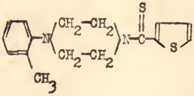
Graphic Formula:



Reactants:	1-(*o*-Tolyl)piperazine	17.0 ml., 17.6 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		56
Molecular Formula		$C_{18}H_{20}N_2S$
Molecular Weight		296.42
Melting Point		116.2-117.2
Analyses:	Carbon, %	Calcd., 72.93; Found, 73.09
	Hydrogen, %	Calcd., 6.80; Found, 6.48
Crystals (yellow plates)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*o*-Tolyl)-4-(thio-2-thenoyl)piperazine

Graphic Formula:



Reactants:

1-(*o*-Tolyl)piperazine	17.0 ml., 17.6 g.
Thiophene aldehyde	9.2 ml., 11.2 g.
Sulfur	3.2 g.

Reaction Solvent . . . . .Pyridine

Yield, % 66

Molecular Formula . . . . $C_{16}H_{18}N_2S_2$

Molecular Weight 302.44

Melting Point 129.3-130.3

Analyses:

Carbon, %	Calcd., 63.54; Found, 64.51
Hydrogen, %	Calcd., 6.00; Found, 6.17

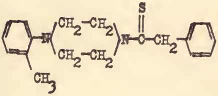
Crystals (shiny, green-gold plates) . . . . **from Acetone-Ethanol**

Solubilities:

Moderately soluble in	Acetone
Slightly soluble in	Ethanol
Very slightly soluble in	Heptane
Insoluble in	**Water**

1-(*o*-Tolyl)-4-(phenylthioacetyl)piperazine

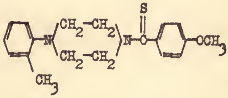
Graphic Formula:



Reactants:	1-(*o*-Tolyl)piperazine	17.0 ml., 17.6 g.
	Acetophenone	11.6 ml., 12.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		61
Molecular Formula		$C_{19}H_{22}N_2S$
Molecular Weight		310.45
Melting Point		107.6-108.6
Analyses:	Carbon, %	Calcd., 73.50; Found, 74.12
	Hydrogen, %	Calcd., 7.14; Found, 6.70
Crystals (pale ivory powder)		from Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(*o*-Tolyl)-4-(thio-*p*-anisoyl)piperazine

Graphic Formula:



Reactants:	1-(*o*-Tolyl)piperazine	17.0 ml., 17.6 g.
	p-Anisaldehyde	12.1 ml., 13.6 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	71
Molecular Formula	$C_{19}H_{22}ON_2S$
Molecular Weight	326.45
Melting Point	118.2-119.2

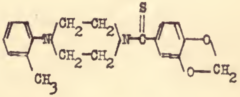
Analyses:	Carbon, %	Calcd., 69.90; Found, 69.74
	Hydrogen, %	Calcd., 6.79; Found, 6.71

Crystals (pale ivory powder)	from Acetone-Water

Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(o-Tolyl)-4-(thiopiperonyloyl)piperazine

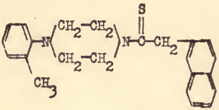
Graphic Formula:



Reactants:	1-(o-Tolyl)piperazine	17.0 ml., 17.6 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		79
Molecular Formula		$C_{19}H_{20}O_2N_2S$
Molecular Weight		340.43
Melting Point		143.5-144.5
Analyses:	Carbon, %	Calcd., 67.03; Found, 67.30
	Hydrogen, %	Calcd., 5.92; Found, 5.83
Crystals (pale ivory powder)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(o-Tolyl)-4-(2-naphthylthioacetyl)piperazine

Graphic Formula:



Reactants:	1-(o-Tolyl)piperazine	17.0 ml., 17.6 g.
	2-Acetonaphthone	17.0 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	38
Molecular Formula	$C_{23}H_{24}N_2S$
Molecular Weight	360.50
Melting Point	148.6-149.6

Analyses:	Carbon, %	Calcd., 76.62; Found, 77.11
	Hydrogen, %	Calcd., 6.71; Found, 6.80

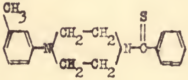
Crystals (shiny, ivory needles)	from Acetone-Ethanol

Solubilities:

Slightly soluble in	Acetone
Very slightly soluble in	Ethanol
Insoluble in	Water

1-(m-Tolyl)-4-(thiobenzoyl)piperazine

Graphic Formula:



Reactants:	1-(m-Tolyl)piperazine	17.0 ml., 17.6 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 77

Molecular Formula . . . . $C_{18}H_{20}N_2S$

Molecular Weight 296.42

Melting Point 82.9-83.9

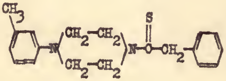
Analyses:	Carbon, %	Calcd., 72.93;	Found, 73.26
	Hydrogen, %	Calcd., 6.80;	Found, 6.49

Crystals (pale yellow powder) . . . . from Ethanol

Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*m*-Tolyl)-4-(phenylthioacetyl)piperazine

Graphic Formula:



Reactants: 1-(*m*-Tolyl)piperazine . . . . . 17.0 ml., 17.6 g.
Acetophenone . . . . 11.6 ml., 12.0 g.
Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 52

Molecular Formula . . . . $C_{19}H_{22}N_2S$

Molecular Weight 310.45

Melting Point 85.1-86.1

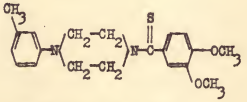
Analyses: Carbon, % . . . . . . Calcd., 73.50; Found, 72.96
Hydrogen, % . . . . . Calcd., 7.14; Found, 6.99

Crystals (lustrous ivory flakes) . . . . from Ethanol

Solubilities: Soluble in . . . . Acetone
Moderately soluble in . . . . Ethanol
Slightly soluble in . . . . Heptane
Insoluble in . . . . Water

1-(*m*-Tolyl)-4-(thioveratroyl)piperazine

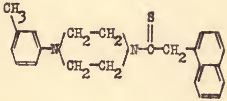
Graphic Formula:



Reactants:	1-(*m*-Tolyl)piperazine	17.0 ml., 17.6 g.
	Veratraldehyde	16.7 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		77
Molecular Formula		$C_{20}H_{24}O_2N_2S$
Molecular Weight		356.47
Melting Point		157.2-158.2
Analyses:	Carbon, %	Calcd., 67.38; Found, 67.41
	Hydrogen, %	Calcd., 6.79; Found, 6.89
Crystals (lustrous pale yellow plates)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*m*-Tolyl)-4-(1-naphthylthioacetyl)piperazine

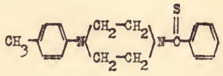
Graphic Formula:



Reactants:	1-(*m*-Tolyl)piperazine	17.0 ml., 17.6 g.
	1-Acetonaphthone	16.0 ml., 17.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		33
Molecular Formula		$C_{23}H_{24}N_2S$
Molecular Weight		360.50
Melting Point		159.7-160.7
Analyses:	Carbon, %	Calcd., 76.62; Found, 76.49
	Hydrogen, %	Calcd., 6.71; Found, 6.52
Crystals (lustrous pale yellow flakes)		from Acetone-Ethanol
Solubilities:	Slightly soluble in	Acetone
	Very slightly soluble in	Ethanol
	Insoluble in	Water

1-(p-Tolyl)-4-(thiobenzoyl)piperazine

Graphic Formula:



Reactants:	1-(p-Tolyl)piperazine	17.0 ml., 17.6 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 84

Molecular Formula . . . . $C_{18}H_{20}N_2S$

Molecular Weight 296.42

Melting Point 137.4-138.4

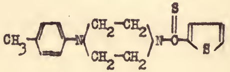
Analyses:	Nitrogen, %	Calcd., 9.45	Found, 9.35
	Sulfur, %	Calcd., 10.82	Found, 10.75

Crystals (shiny, light yellow plates) . . . . from Propanol-2

Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(*p*-Tolyl)-4-(thio-2-thenoyl)piperazine

Graphic Formula:



Reactants: 1-(*p*-Tolyl)piperazine . . . . . 17.0 ml., 17.6 g.

Thiophene aldehyde . . . . 9.2 ml., 11.2 g.

Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 55

Molecular Formula . . . . $C_{16}H_{18}N_2S_2$

Molecular Weight 302.44

Melting Point 122.2-123.2

Analyses: Carbon, % . . . . . . Calcd., 63.54; Found, 64.05

Hydrogen, % . . . . . Calcd., 6.00; Found, 5.98

Crystals (fine, orange needles) . . . . from Acetone-Ethanol

Solubilities: Moderately soluble in . . . . Acetone

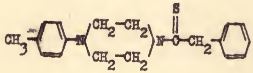
Slightly soluble in . . . . Ethanol

Very slightly soluble in . . . . Heptane

Insoluble in . . . . Water

1-(*p*-Tolyl)-4-(phenylthioacetyl)piperazine

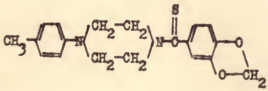
Graphic Formula:



Reactants:	1-(*p*-Tolyl)piperazine	17.0 ml., 17.6 g.
	Acetophenone	11.6 ml., 12.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		32
Molecular Formula		$C_{19}H_{22}N_2S$
Molecular Weight		310.45
Melting Point		106.1-107.1
Analyses:	Carbon, %	Calcd., 73.50; Found, 73.64
	Hydrogen, %	Calcd., 7.14; Found, 6.53
Crystals (lustrous pale yellow flakes)		from Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(p-Tolyl)-4-(thiopiperonyloyl)piperazine

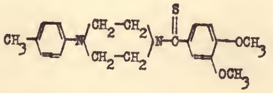
Graphic Formula:



Reactants:	1-(p-Tolyl)piperazine	17.0 ml., 17.6 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		65
Molecular Formula		$C_{19}H_{20}O_2N_2S$
Molecular Weight		340.43
Melting Point		134.3-135.3 (Softens at 127)
Analyses:	Carbon, %	Calcd., 67.03; Found, 67.20
	Hydrogen, %	Calcd., 5.92; Found, 6.04
Crystals (bright yellow powder)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(p-Tolyl)-4-(thioveratroyl)piperazine

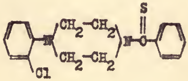
Graphic Formula:



Reactants:	1-(p-Tolyl)piperazine	17.0 ml., 17.6 g.
	Veratraldehyde	16.7 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		94
Molecular Formula		$C_{20}H_{24}O_2N_2S$
Molecular Weight		356.47
Melting Point		153.7-154.7
Analyses:	Carbon, %	Calcd., 67.38; Found, 67.60
	Hydrogen, %	Calcd., 6.79; Found, 7.40
Crystals (shiny yellow flakes)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(o-Chlorophenyl)-4-(thiobenzoyl)piperazine

Graphic Formula:



Reactants:	1-(o-Chlorophenyl)piperazine	17.0 ml., 19.7 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 86

Molecular Formula . . . . $C_{17}H_{17}N_2SCl$

Molecular Weight 316.85

Melting Point 120.7-121.2

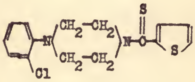
Analyses:	Chlorine, %	Calcd., 11.19; Found, 11.60
	Nitrogen, %	Calcd., 8.84; Found, 8.63

Crystals (shiny yellow plates) . . . . from Propanol-2

Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(*o*-Chlorophenyl)-4-(thio-2-thenoyl)piperazine

Graphic Formula:



Reactants: 1-(*o*-Chlorophenyl)piperazine . . 17.0 ml., 19.7 g.

Thiophene aldehyde . . . . 9.2 ml., 11.2 g.

Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 54

Molecular Formula . . . . $C_{15}H_{15}N_2S_2Cl$

Molecular Weight 322.87

Melting Point 123.2-124.2

Analyses: Carbon, % . . . . . . Calcd., 55.80; Found, 56.62

Hydrogen, % . . . . . Calcd., 4.68; Found, 4.98

Crystals (lustrous orange plates) . . . . from Acetone-Ethanol

Solubilities: Moderately soluble in . . . . Acetone

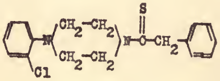
Slightly soluble in . . . . Ethanol

Very slightly soluble in . . . . Heptane

Insoluble in . . . . Water

1-(*o*-Chlorophenyl)-4-(phenylthioacetyl)piperazine

Graphic Formula:



Reactants:	1-(*o*-Chlorophenyl)piperazine	17.0 ml., 19.7 g.
	Acetophenone	11.6 ml., 12.0 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	33
Molecular Formula	$C_{18}H_{19}N_2SCl$
Molecular Weight	330.81
Melting Point	103.1-104.1

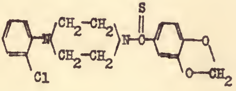
Analyses:	Carbon, %	Calcd., 65.34;	Found, 66.04
	Hydrogen, %	Calcd., 5.79;	Found, 6.14

Crystals (pale yellow powder)	from Ethanol

Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(o-Chlorophenyl)-4-(thiopiperonyloyl)piperazine

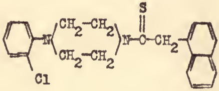
Graphic Formula:



Reactants:	1-(o-Chlorophenyl)piperazine	17.0 ml., 19.7 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		71
Molecular Formula		$C_{18}H_{17}O_2N_2SCl$
Molecular Weight		360.86
Melting Point		123.8-124.8
Analyses:	Carbon, %	Calcd., 59.91; Found, 60.18
	Hydrogen, %	Calcd., 4.75; Found, 5.03
Crystals (shiny, pale yellow plates)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(o-Chlorophenyl)-4-(1-naphthylthioacetyl)piperazine

Graphic Formula:



Reactants:	1-(o-Chlorophenyl)piperazine	17.0 ml., 19.7 g.
	1-Acetonaphthone	16.0 ml., 17.0 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	4
Molecular Formula	$C_{22}H_{21}N_2SCl$
Molecular Weight	380.93
Melting Point	139.5-141.5

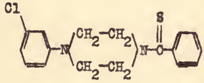
Analyses:	Carbon, %	Calcd., 69.36; Found, 68.28
	Hydrogen, %	Calcd., 5.56; Found, 5.64

Crystals (ivory powder)	from Acetone-Ethanol

Solubilities:	Slightly soluble in	Acetone
	Very slightly soluble in	Ethanol
	Insoluble in	Water

1-(m-Chlorophenyl)-4-(thiobenzoyl)piperazine

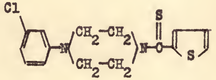
Graphic Formula:



Reactants:	1-(m-Chlorophenyl)piperazine	16.5 ml., 19.7 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		49
Molecular Formula		$C_{17}H_{17}N_2SCl$
Molecular Weight		316.85
Melting Point		100-101
Analyses:	Carbon, %	Calcd., 64.44; Found, 64.61
	Hydrogen, %	Calcd., 5.41; Found, 4.90
Crystals (ivory-yellow powder)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*m*-Chlorophenyl)-4-(thio-2-thenoyl)piperazine

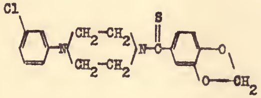
Graphic Formula:



Reactants:	1-(*m*-Chlorophenyl)piperazine	16.5 ml., 19.7 g.
	Thiophene aldehyde	9.2 ml., 11.2 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		51
Molecular Formula		$C_{15}H_{15}N_2S_2Cl$
Molecular Weight		322.87
Melting Point		95-96
Analyses:	Carbon, %	Calcd., 55.80; Found, 55.62
	Hydrogen, %	Calcd., 4.68; Found, 4.70
Crystals (lustrous orange plates)		from Acetone-Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(m-Chlorophenyl)-4-(thiopiperonyloyl)piperazine

Graphic Formula:



Reactants:		
	1-(m-Chlorophenyl)piperazine	16.5 ml., 19.7 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	80
Molecular Formula	$C_{18}H_{17}O_2N_2SCl$
Molecular Weight	360.86
Melting Point	114.1-115.1

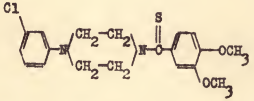
Analyses:		
	Carbon, %	Calcd., 59.91; Found, 59.93
	Hydrogen, %	Calcd., 4.75; Found, 4.76

Crystals (yellow powder)	from Ethanol

Solubilities:		
	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*m*-Chlorophenyl)-4-(thioveratroyl)piperazine

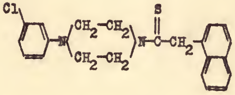
Graphic Formula:



Reactants:	1-(*m*-Chlorophenyl)piperazine	16.5 ml., 19.7 g.
	Veratraldehyde	16.7 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		96
Molecular Formula		$C_{19}H_{21}O_2N_2SCl$
Molecular Weight		376.90
Melting Point		157.2-158.7
Analyses:	Carbon, %	Calcd., 60.54; Found, 60.50
	Hydrogen, %	Calcd., 5.62; Found, 5.69
Crystals (shiny yellow plates)		from Ethanol
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(m-Chlorophenyl)-4-(1-naphthylthioacetyl)piperazine

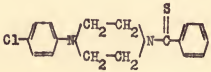
Graphic Formula:



Reactants:	1-(m-Chlorophenyl)piperazine	16.5 ml., 19.7 g.
	1-Acetonaphthone	16.0 ml., 17.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		13
Molecular Formula		$C_{22}H_{21}N_2SCl$
Molecular Weight		380.93
Melting Point		122.2-123.2
Analyses:	Carbon, %	Calcd., 69.36; Found, 68.38
	Hydrogen, %	Calcd., 5.56; Found, 5.78
Crystals (pale yellow powder)		from Acetone-Ethanol
Solubilities:	Slightly soluble in	Acetone
	Very slightly soluble in	Ethanol
	Insoluble in	Water

1-(p-Chlorophenyl)-4-(thiobenzoyl)piperazine

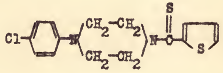
Graphic Formula:



Reactants:	1-(p-Chlorophenyl)piperazine	19.7 g.
	Benzaldehyde	10.1 ml., 10.6 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		49
Molecular Formula		$C_{17}H_{17}N_2SCl$
Molecular Weight		316.85
Melting Point		115.1-116.1
Analyses:	Carbon, %	Calcd., 64.44; Found, 64.44
	Hydrogen, %	Calcd., 5.41; Found, 5.16
Crystals (bright yellow powder)		from Acetone
Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(p-Chlorophenyl)-4-(thio-2-thenoyl)piperazine

Molecular Formula:



Reactants:	1-(p-Chlorophenyl)piperazine	19.7 g.
	Thiophene aldehyde	9.2 ml., 11.2 g.
	Sulfur	3.2 g.

Reaction Solvent	Pyridine
Yield, %	48
Molecular Formula	$C_{15}H_{15}N_2S_2Cl$
Molecular Weight	322.87
Melting Point	155.7-157.2

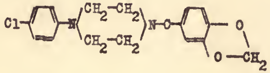
Analyses:	Carbon, %	Calcd., 55.80; Found, 56.14
	Hydrogen, %	Calcd., 4.68; Found, 4.74

Crystals (lustrous, deep orange plates) . . . . . from Acetone-Ethanol

Solubilities:	Moderately soluble in	Acetone
	Slightly soluble in	Ethanol
	Very slightly soluble in	Heptane
	Insoluble in	Water

1-(*p*-Chlorophenyl)-4-(thiopiperonyloyl)piperazine

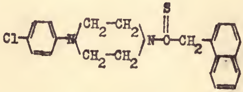
Graphic Formula:



Reactants:	1-(*p*-Chlorophenyl)piperazine	19.7 g.
	Piperonal	15.0 g.
	Sulfur	3.2 g.
Reaction Solvent		Pyridine
Yield, %		62
Molecular Formula		$C_{18}H_{17}O_2N_2SCl$
Molecular Weight		360.86
Melting Point		130.3-131.3
Analyses:	Carbon, %	Calcd., 59.91; Found, 60.48
	Hydrogen, %	Calcd., 4.75; Found, 4.42
Crystals (yellow powder)		from Ethanol
Solubilities:	Soluble in	Acetone
	Moderately soluble in	Ethanol
	Slightly soluble in	Heptane
	Insoluble in	Water

1-(*p*-Chlorophenyl)-4-(1-naphthylthioacetyl)piperazine

Graphic Formula:



Reactants: 1-(*p*-Chlorophenyl)piperazine . . . . 19.7 g.

1-Acetonaphthone . . . . 16.0 ml., 17.0 g.

Sulfur . . . . 3.2 g.

Reaction Solvent . . . . Pyridine

Yield, % 3

Molecular Formula . . . . $C_{22}H_{21}N_2SCl$

Molecular Weight 380.93

Melting Point 146.5-147.5
(Softens at 126)

Analyses: Carbon, % . . . . . . Calcd., 69.36; Found, 68.48

Hydrogen, % . . . . . Calcd., 5.56; Found, 5.62

Crystals (light yellow powder) . . . . from Acetone-Ethanol

Solubilities: Slightly soluble in . . . . Acetone

Very slightly soluble in . . . . Ethanol

Insoluble in . . . . Water

CHAPTER III

SUMMARY

Forty-seven new thioamides have been prepared by the Kindler Modification of the Willgerodt reaction.

A review of literature on the reaction has been presented. The possible mechanisms which have been proposed by various authors have been reviewed.

An individual sheet, tabulating significant data, has been prepared for each of the thioamides; complete description of methods of preparation and purification precedes these sheets.

Physical and analytical data for the new compounds are presented in Table I.

TABLE I

Physical and Analytical Data of Thioamides from Piperazines

Derivative, piperazine	Molecular Formula	M.p., °C. (Corr.)	Yield, %	Analyses				
				Carbon, %		Hydrogen, %		Others
				Calcd.	Found	Calcd.	Found	
1-Phenyl-4-(thiobutanoyl)-	$C_{14}H_{20}N_2S$	66.8- 67.8	29	...	...	...	...	N,%: Calcd.,11.28; Found, 11.35
1-Phenyl-4-(thioisobutanoyl)-	$C_{14}H_{20}N_2S$	62.7- 63.7	50	...	...	...	...	N,%: Calcd.,11.28; Found, 11.12
1-Phenyl-4-(thiopentanoyl)-	$C_{15}H_{22}N_2S$	47.5- 48.5	13	68.65	68.82	8.45	8.52	
1-Phenyl-4-(thiohexanoyl)-	$C_{16}H_{24}N_2S$	62.7- 63.7	14	69.51	69.75	8.75	8.77	
1-Phenyl-4-(2-ethylthiobutanoyl)-	$C_{16}H_{24}N_2S$	94.0- 95.0	30	69.51	69.70	8.75	8.70	
1-Phenyl-4-(4-methylthiopentanoyl)-	$C_{16}H_{24}N_2S$	77.8- 78.8	5	69.51	68.84	8.75	8.65	
1-Phenyl-4-(thioheptanoyl)-	$C_{17}H_{26}N_2S$	62.7- 63.7	14	70.29	70.57	9.02	8.82	
1-Phenyl-4-(thioöctanoyl)-	$C_{18}H_{28}N_2S$	48.5- 49.5	25	71.00	70.98	9.27	9.30	
1-Phenyl-4-(thiononanoyl)-	$C_{19}H_{30}N_2S$	52.6- 53.6	28	71.64	71.41	9.49	9.21	
1-Phenyl-4-(thiodecanoyl)-	$C_{20}H_{32}N_2S$	51.6- 52.6	36	72.23	71.90	9.70	9.85	
1-Phenyl-4-(thiobenzoyl)-	$C_{17}H_{18}N_2S$	93.5- 94.5	83	...	...	...	...	N,%: Calcd., 9.92; Found, 9.73 S,%: Calcd.,11.35; Found, 11.75

TABLE I (Continued)

Derivative, piperazine	Molecular Formula	M.p., °C. (Corr.)	Yield, %	Analyses				
				Carbon, %		Hydrogen, %		Others
				Calcd.	Found	Calcd.	Found	
1-Phenyl-4-(thio-2-thenoyl)-	$C_{15}H_{16}N_2S_2$	106.1-107.1	35	62.46	62.75	5.59	5.71	N,%: Calcd., 9.71; Found, 9.45
1-Phenyl-4-(phenylthioacetyl)-	$C_{18}H_{20}N_2S$	125.2-126.2	62	...	...	...	...	N,%: Calcd., 9.45; Found, 9.42
1-Phenyl-4-(thio-*p*-anisoyl)-	$C_{18}H_{20}ON_2S$	160.2-161.7	61	69.19	69.75	6.45	6.64	
1-Phenyl-4-(thiopiperonyloyl)-	$C_{18}H_{18}O_2N_2S$	130.3-131.3	65	...	...	...	...	N,%: Calcd., 8.58; Found, 8.76
1-Phenyl-4-(thioveratroyl)-	$C_{19}H_{22}O_2N_2S$	160.7-162.7	70	66.63	67.01	6.48	6.66	
1-Phenyl-4-(1-naphthylthioacetyl)-	$C_{22}H_{22}N_2S$	134.7-136.2	14	...	...	...	...	N,%: Calcd., 8.09; Found, 8.29
1-(*o*-Tolyl)-4-(thiobutanoyl)-	$C_{15}H_{22}N_2S$	71.8- 72.8	38	68.65	67.84	8.45	8.35	
1-(*o*-Tolyl)-4-(thiobenzoyl)-	$C_{18}H_{20}N_2S$	116.2-117.2	56	72.93	73.09	6.80	6.48	
1-(*o*-Tolyl)-4-(thio-2-thenoyl)-	$C_{16}H_{18}N_2S_2$	129.3-130.3	66	63.54	64.51	6.00	6.17	
1-(*o*-Tolyl)-4-(phenylthioacetyl)-	$C_{19}H_{22}N_2S$	107.6-108.6	61	73.50	74.12	7.14	6.70	
1-(*o*-Tolyl)-4-(thio-*p*-anisoyl)-	$C_{19}H_{22}ON_2S$	118.2-119.2	71	69.90	69.74	6.79	6.71	
1-(*o*-Tolyl)-4-(thiopiperonyloyl)-	$C_{19}H_{20}O_2N_2S$	143.5-144.5	79	67.03	67.30	5.92	5.83	

TABLE I (Continued)

Derivative, piperazine	Molecular Formula	M.p., °C. (Corr.)	Yield, %	Analyses Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Others
1-(*o*-Tolyl)-4-(2-naphthylthioacetyl)-	$C_{23}H_{24}N_2S$	148.6-149.6	38	76.62	77.11	6.71	6.80	
1-(*m*-Tolyl)-4-(thiobenzoyl)-	$C_{18}H_{20}N_2S$	82.9- 83.9	77	72.93	73.26	6.80	6.49	
1-(*m*-Tolyl)-4-(phenylthioacetyl)-	$C_{19}H_{22}N_2S$	85.1- 86.1	52	73.50	72.96	7.14	6.99	
1-(*m*-Tolyl)-4-(thioveratroyl)-	$C_{20}H_{24}O_2N_2S$	157.2-158.2	77	67.38	67.41	6.79	6.89	
1-(*m*-Tolyl)-4-(1-naphthylthioacetyl)-	$C_{23}H_{24}N_2S$	159.7-160.7	33	76.62	76.49	6.71	6.52	
1-(*p*-Tolyl)-4-(thiobenzoyl)-	$C_{18}H_{20}N_2S$	137.4-138.4	84	...	...	...	...	N,%: Calcd., 9.45; Found, 9.35 S,%: Calcd., 10.82; Found, 10.75
1-(*p*-Tolyl)-4-(thio-2-thenoyl)-	$C_{16}H_{18}N_2S_2$	122.2-123.2	55	63.54	64.05	6.00	5.98	
1-(*p*-Tolyl)-4-(phenylthioacetyl)-	$C_{19}H_{22}N_2S$	106.1-107.1	32	73.50	73.64	7.14	6.53	
1-(*p*-Tolyl)-4-(thiopiperonyloyl)-	$C_{19}H_{20}O_2N_2S$	134.3-135.3	65	67.03	67.20	5.92	6.04	
1-(*p*-Tolyl)-4-(thioveratroyl)-	$C_{20}H_{24}O_2N_2S$	153.7-154.7	94	67.38	67.60	6.79	7.40	
1-(*o*-Chlorophenyl)-4-(thiobenzoyl	$C_{17}H_{17}N_2SCl$	120.7-121.7	86	...	...	...	...	N,%: Calcd., 8.84; Found, 8.63 Cl,%: Calcd., 11.19; Found, 11.60

TABLE I (Continued)

Derivative, piperazine	Molecular Formula	M.p., °C. (Corr.)	Yield, %	Analyses				
				Carbon, %		Hydrogen, %		Others
				Calcd.	Found	Calcd.	Found	
1-(o-Chlorophenyl)-4-(thio-2-thenoyl)-	$C_{15}H_{15}N_2S_2Cl$	123.2-124.2	54	55.80	56.62	4.68	4.98	
1-(o-Chlorophenyl)-4-(phenylthioacetyl)-	$C_{18}H_{19}N_2SCl$	103.1-104.1	33	65.34	66.04	5.79	6.14	
1-(o-Chlorophenyl)-4-(thiopiperonyloyl)-	$C_{18}H_{17}O_2N_2SCl$	123.8-124.8	71	59.91	60.18	4.75	5.03	
1-(o-Chlorophenyl)-4-(1-naphthylthioacetyl)-	$C_{22}H_{21}N_2SCl$	139.5-141.5	4	69.36	68.28	5.56	5.64	
1-(m-Chlorophenyl)-4-(thiobenzoyl)-	$C_{17}H_{17}N_2SCl$	100.0-101.0	49	64.44	64.61	5.41	4.90	
1-(m-Chlorophenyl)-4-(thio-2-thenoyl)-	$C_{15}H_{15}N_2S_2Cl$	95.0- 96.0	51	55.80	55.62	4.68	4.70	
1-(m-Chlorophenyl)-4-(thiopiperonyloyl)-	$C_{18}H_{17}O_2N_2SCl$	114.1-115.1	80	59.91	59.93	4.75	4.76	
1-(m-Chlorophenyl)-4-(thioveratroyl)-	$C_{19}H_{21}O_2N_2SCl$	157.2-158.7	96	60.54	60.50	5.62	5.69	
1-(m-Chlorophenyl)-4-(1-naphthylthioacetyl)-	$C_{22}H_{21}N_2SCl$	122.2-123.2	13	69.36	68.38	5.56	5.78	
1-(p-Chlorophenyl)-4-(thiobenzoyl)-	$C_{17}H_{17}N_2SCl$	115.1-116.1	49	64.44	64.44	5.41	5.16	
1-(p-Chlorophenyl)-4-(thio-2-thenoyl)-	$C_{15}H_{15}N_2S_2Cl$	155.7-157.2	48	55.80	56.14	4.68	4.74	
1-(p-Chlorophenyl)-4-(thiopiperonyloyl)-	$C_{18}H_{17}O_2N_2SCl$	130.3-131.3	62	59.91	60.48	4.75	4.42	
1-(p-Chlorophenyl)-4-(1-naphthylthioacetyl)-	$C_{22}H_{21}N_2SCl$	146.5-147.5	3	69.36	68.48	5.56	5.62	

BIBLIOGRAPHY

1. R. T. Arnold, E. Schultz, and H. Klug, J. Am. Chem. Soc., 66, 1606-7(1944).

2. Y. A. Baskakov and N. N. Mel'nikov, Zhur. Obshchei Khim., 23, 865-8(1953).

3. E. Baumann and E. Fromm, Ber., 28, 890(1895).

4. R. Boudet, Ann. chim., (12) 10, 178(1955).

5. E. V. Brown, E. Cerwonka, and R. C. Anderson, J. Am. Chem. Soc., 73, 3735-8(1951).

6. A. Cahours, Compt. rend., 27, 239(1848).

7. M. Carmack and DeLos F. DeTar, J. Am. Chem. Soc., 68, 2029(1946).

8. M. Carmack and DeLos F. DeTar, U. S. Pat. 2,495,567, Jan. 24, 1950.

9. M. Carmack and M. A. Spielman, "Organic Reactions," Vol. III. New York: John Wiley and Sons, 1949. Pp. 83-107.

10. L. Cavalieri, D. B. Pattison, and M. Carmack, J. Am. Chem. Soc., 67, 1783(1945).

11. E. Cerwonka, R. C. Anderson, and E. V. Brown, ibid., 75, 28-30 (1953).

12. P. Chabrier and S-T. Renard, Compt. rend., 228, 850-2(1949).

13. W. G. Dauben, J. C. Reid, P. E. Yankwich, and M. Calvin, J. Am. Chem. Soc., 72, 121-4(1950).

14. DeLos F. DeTar and M. Carmack, ibid., 68, 2025(1946).

15. J. Dumas, Ann. chim. et phys., (2) 44, 129(1830).

16. B. Emmert and M. Groll, Ber., 86, 205-8(1953).

17. L. F. Fieser and G. W. Kilmer, J. Am. Chem. Soc., 62, 1354(1940).

18. W. T. Forsee, Jr., and C. B. Pollard, ibid., 57, 1788(1935).

19. R. T. Gerry and E. V. Brown, *J. Am. Chem. Soc.*, *75*, 750-1(1953).

20. Y. Hara and S. Fujise, *J. Chem. Soc. Japan*, Pure Chem. Sect., *74*, 698-9(1953).

21. M. Hartmann and W. Bosshard, *Helv. Chim. Acta*, *24*, 28E(1941).

22. K. Kindler, Ger. Pat. 385,376, Nov. 23, 1923.

23. K. Kindler, *Ann. Chem., Justus Liebigs*, *431*, 193, 222(1923).

24. K. Kindler, *Arch. Pharm.*, *265*, 389(1927).

25. K. Kindler and T. Li, *Ber.*, *74*, 321(1941).

26. J. A. King and F. H. McMillan, *J. Am. Chem. Soc.*, *68*, 525(1946).

27. *Ibid.*, *68*, 632 (1946).

28. *Ibid.*, *68*, 1369-73(1946).

29. *Ibid.*, *68*, 2335-9(1946).

30. *Ibid.*, *69*, 1207-8(1947).

31. *Ibid.*, *70*, 4143(1948).

32. J. A. King and F. H. McMillan, U. S. Pat. 2,468,011, Sept.18, 1951.

33. M. A. Naylor, Jr., U. S. Pat. 2,610,980, Sept. 16, 1952.

34. A. C. Ott, L. A. Mattano and G. A. Coleman, *J. Am. Chem. Soc.*, *68*, 2633(1946).

35. D. B. Pattison and M. Carmack, *ibid.*, *68*, 2033(1946).

36. C. B. Pollard and L. G. MacDowell, *ibid.*, *57*, 2363(1935).

37. C. B. Pollard and T. H. Wicker, Jr., *ibid.*, *76*, 1853-5(1954).

38. H. D. Porter, *ibid.*, *76*, 127(1954).

39. E. Schwenck and E. Bloch, *ibid.*, *64*, 3051(1942).

40. C. Thomae, *Arch. Pharm.*, *244*, 643(1906).

41. O. Wallach, *Ann. Chem., Justus Liebigs*, *259*, 300 (1890).

42. C. Willgerodt, *Ber.*, *20*, 2467(1887); *21*, 534(1888).

43. C. Willgerodt, *J. prakt. Chem.*, (2) *80*, 183(1909).

44. C. Willgerodt and W. Hambrecht, *ibid.*, (2) *81*, 74(1910).

45. C. Willgerodt and F. H. Merk, *ibid.*, (2) *80*, 192(1909).

46. Y. Yukawa and Y. Kishi, *J. Chem. Soc. Japan*, Pure Chem. Sect., *72*, 371-3(1951).

47. Y. Yukawa, F. Tokuda, and S. Amano, *ibid.*, *73*, 498-501(1952).

BIOGRAPHICAL ITEMS

John C. Braun was born in Kimball, South Dakota, on June 9, 1917. He grew up on a farm in central Minnesota and was graduated from Pillager, Minnesota, High School in 1933. He moved to Florida in 1936 and farmed there with his father until 1941.

In 1941 he enlisted in the Army Air Corps. He was an airplane mechanic, then a flight engineer on a B-29 bomber. He received the Air Medal with two oak-leaf clusters for bombing missions from Guam over Japan. He was discharged in 1945 with the rank of Technical Sergeant.

He entered the University of Florida in 1946 and received the Certificate of Associate of Arts, with High Honors, in 1947 and was graduated, with honors, in 1949, with the degree of Bachelor of Science in Chemistry.

He was elected to Phi Eta Sigma, Freshman Honorary; Gamma Sigma Epsilon, Honorary Chemical; Delta Phi Alpha, Honorary German; and Phi Kappa Phi scholastic societies.

He entered Graduate School at the University of Florida in February, 1950, and received the degree of Doctor of Philosophy in August, 1955.

While attending the University he served as Student Assistant in the German Department and as Graduate Assistant and Teaching Assistant in the Department of Chemistry. He held a Parke-Davis Research Fellowship for almost three years.

He is married and has one daughter.

ACKNOWLEDGEMENTS

The author wishes to express his gratitude to the many faculty members of the Chemistry, Physics, Foreign Languages and Mathematics Departments who have helped make his stay at the University an interesting and worthwhile one. He also appreciates the help of his Supervisory Committee.

He is especially grateful to Dr. C. B. Pollard for moral support, technical advice and assistance in obtaining Graduate and Teaching Assistantships and for appointment as a Parke-Davis Research Fellow.

He appreciates the assistance Parke, Davis & Company has provided in furnishing a Research Grant for work under Dr. Pollard's direction.

He wishes to thank his fellow graduate students who, by their advice, co-operation and help in solving various technical problems and by their friendship, made his work easier and life more interesting.

He is grateful to Mr. Workinger and Mr. Mixon, who helped him procure various equipment needed in his work, and to Mr. Thompson, for his assistance and for teaching him the elements of glass-working.

He also appreciates the help of his wife, who offered encouragement when things looked dark and who helped immeasurably in the preparation, correction and production of this dissertation.

COMMITTEE REPORT

This dissertation was prepared under the direction of the Chairman of the candidate's Supervisory Committee and has been approved by all members of the Committee. It was submitted to the Dean of the College of Arts and Sciences and to the Graduate Council and was approved as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Date

C. F. Byers
Dean, College of Arts and Sciences

Dean, Graduate School

SUPERVISORY COMMITTEE:

C. B. Pollard
Chairman

C. E. Reid

J. E. Hawkins

A. H. Gropp

D. C. Swanson